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CLAIMS:

1. Use of an 8.9 cM region of human chromosome 18q disposed between polymorphic markers D18S68 and D18S979 or a fragment thereof for identifying at least one human gene, including mutated or polymorphic variants thereof, which is associated with a mood disorder or related disorder.

2. Use of a YAC clone comprising a portion of human chromosome 18q disposed between polymorphic markers D18S60 and D18S61 for identifying at least one human gene, including mutated or polymorphic variants thereof, which is associated with a mood disorder or related disorder.

3. The use as claimed in claim 2 wherein said portion comprises the region of chromosome 18q between polymorphic markers D18S68 and D18S979 or a fragment of said region.

4. The use as claimed in claim 2 or 3 wherein said YAC clone is 961.h.9, 942.c.3, 766.f.12, 731.c.7, 907.e.1, 752-g-8 or 717.d.3.

5. The use as claimed in claim 4 wherein said YAC clone is 961.h.9, 766.f.12 or 907.e.1.

6. The use as claimed in ~~any preceding claim~~ _claim 1_ wherein said mood disorder or related disorder is selected from the Diagnostic and Statistical Manual of Mental Disorders, version 4 (DSM-IV) taxonomy and includes mood disorders (296.XX, 300.4, 311, 301, 13, 295.70), schizophrenia and related disorders (295, 297.1, 298.9, 297.3, 298.9), anxiety disorders

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(300.XX, 309.81, 308.3), adjustment disorders (309, XX) and personality disorders (codes 301. XX).

7. A method of identifying at least one human gene, including mutated or polymorphic variants thereof, which is associated with a mood disorder or related disorder which comprises detecting nucleotide triplet repeats in a region of human chromosome 18q disposed between polymorphic markers D18S68 and D18S979.

8. A method of identifying at least one human gene, including mutated or polymorphic variants thereof, which is associated with a mood disorder or related disorder which comprises fragmentation of a YAC clone as defined in any one of claims 2 to 4 and detection of nucleotide triplet repeats.

9. A method as claimed in claim 7 or 8 wherein said repeated triplet is CAG or CTG.

10. A method as claimed in claim 9 wherein said repeated triplet is detected by means of a probe comprising at least 5 CTG and/or CAG repeats.

11. A method of identifying at least one human gene including mutated or polymorphic variants thereof, which is associated with a mood disorder or related disorder wherein said gene is present in the DNA comprised in the YAC clones as defined in any one of claims 2 to 5, which method comprises the step of detecting an expression product of said gene with an antibody capable of recognising a protein with an amino acid sequence comprising a string of at least 8 continuous glutamine residues.

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12. A method as claimed in claim 11 wherein said DNA forms part of a human cDNA expression library.

13. A method as claimed in claim 11 ~~or claim 12~~ wherein said antibody is mAB 1C2.

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14. A method of preparing a contig map of YAC clones of the region of human chromosome 18q between polymorphic markers D18S60 and D18S61 which comprises the steps of:

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(a) subcloning the YAC clones according to ~~any one of~~ claims 2 ~~to 5~~ into exon trap vectors;

(b) using the nucleotide sequences shown in any one of Figures 1 to 11 or any other known sequence tagged sequence from the YAC contig described herein, or part thereof consisting of not less than 14 contiguous bases or the complement thereof, to detect overlaps among the cosmid vectors, and

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(c) constructing a cosmid contig map of a YAC clone of said region.

15. A method of identifying at least one human gene or any mutated or polymorphic variant thereof which is associated with a mood disorder or related disorder which comprises the steps of:

25

(a) transfecting mammalian cells with DNA sequences cloned into an exon trap vector as prepared in claim 14;

30

(b) culturing said mammalian cells in an appropriate medium;

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(c) isolating RNA transcripts expressed from an SV40 promoter;

(d) preparing cDNA from said RNA
5   transcripts;

(e) identifying splicing events involving exons of the DNA subcloned into said exon trap vector in accordance with claim 14 to elucidate positions of
10   coding regions in said subcloned DNA;

(f) detecting differences between said coding regions and equivalent regions in the DNA of an individual afflicted with said mood disorder or
15   related disorder; and

(g) identifying said gene or mutated or polymorphic variants thereof which is associated with said mood disorder or related disorder.
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16.   A method of identifying at least one human gene or mutated or polymorphic variants thereof which is associated with a mood disorder or related disorder which comprises the steps of:
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(a) subcloning the YAC clones according to any one of claims 2 to 5 into a cosmid, BAC, PAC or other vector;

30   (b) using the nucleotide sequences shown in any one of Figures 1 to 11 or any other known sequence tagged sequence from the YAC contig described herein, or part thereof consisting of not less than 14 contiguous bases or the complement thereof, to defect
35   overlaps amongst the subclones and construct a map

thereof;

(c) identifying the position of genes within
the subcloned DNA by one or more of CpG island
5   identification, zoo-blotting, hybridization of said
subcloned DNA to a cDNA library or a Northern blot of
mRNA from a panel of culture cell lines;

(d) detecting differences between said genes
10   and equivalent regions of the DNA of an individual
afflicted with a mood disorder or related disorder;
and

(e) identifying said gene which, if
15   defective, is associated with said mood disorder or
related disorder.

17.   An isolated human gene, including mutated or
polymorphic variants thereof, which is associated with
20   a mood disorder or related disorder which is
obtainable by the method according to ~~any of~~ claims 7
~~to 13, 15 or 16~~.

18.   A human protein which, if defective, is
25   associated with a mood disorder or related disorder
which is the expression product of the gene according
to claim 17.

19. A cDNA encoding the protein of claim 18 which
30   is obtainable by the method of ~~any one of~~ claims 7 ~~to
13, 15 or 16~~.

20.   Use of a probe of at least 14 contiguous
nucleotides of the cDNA of claim 19 or the complement
35   thereof in a method for detection in a patient of a

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pathological mutation or genetic variation associated
with a mood disorder or related disorder which method
comprises hybridizing said probe with a sample from
said patient and from a control individual.

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21. A nucleic acid molecule which comprises a
sequence of nucleotides as shown in any one of Figures
15a, 16a, 17a or 18a.

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22. A nucleic acid molecule which comprises a
sequence of nucleotides which differ from a sequence
of nucleotides as shown in any one of Figures 15a,
16a, 17a or 18a only in the extent of trinucleotide
repeats.

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23. A protein encoded by a nucleic acid molecule
as claimed in claim 21.

24. A protein encoded by a nucleic acid molecule
20 as claimed in claim 22.

25. A method of determining the susceptibility
of an individual to a mood disorder or related
disorder which method comprises analysing a sample of
25 DNA from that individual for the presence of a DNA
polymorphism associated with a mood disorder or
related disorder in a region of chromosome 18q
disposed between polymorphic markers D18S68 and
D18S979.

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26. A method as in claims 25 wherein said DNA
polymorphism is a trinucleotide repeat expansion.

27. A method as in claim 26 wherein said
35 trinucleotide repeat expansion is comprised in a

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sequence of nucleotides that differ from the sequence of nucleotides shown in any one of Figures 15a, 16a, 17a or 18a only in said trinucleotide repeat expansion.

5   28. A method as in claim 26 ~~or 27~~ which comprises the steps of:

a) obtaining a DNA sample from said
10 individual;

b) providing primers suitable for the amplification of a nucleotide sequence comprised in the sequence shown in any one of Figures 15a, 16a, 17a
15 or 18a said primers flanking the trinucleotide repeats comprised in said sequence;

c) applying said primers to the said DNA sample and carrying out an amplification reaction;
20

d) carrying out the same amplification reaction on a DNA sample from a control individual; and

25   e) comparing the results of the amplification reaction for the said individual and for the said control individual;

wherein the presence of an amplified
30 fragment from said individual which is bigger in size from that of said control individual is an indication of the presence of a susceptibility to a mood disorder or related disorder of said individual.

35   29. A method as in claim 28 wherein said

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nucleotide sequence to be amplified is comprised in
the sequence shown in Figure 15a and said primers have
the sequences shown in Figure 15b.

5   30.   A method as in claim 28 wherein said
nucleotide sequence to be amplified is comprised in
the sequence shown in Figure 16a and said primers have
the sequences shown in Figure 16b.

10   31.   A method as in claim 28 wherein said
nucleotide sequence to be amplified is comprised in
the sequence shown in Figure 17a and said primers have
the sequences shown in Figure 17b.

15   32.   A method as in claim 28 wherein said
nucleotide sequence to be amplified is comprised in
the sequence shown in Figure 18a and said primers have
the sequences shown in Figure 18b.

20   33.   A method of determining the susceptibility
of an individual to a mood disorder or related
disorder which method comprises the steps of :

         a) obtaining a protein sample from said
25 individual; and

         b) detecting the presence of the protein of
claim 24;

30   wherein the presence of said protein is an
indication of the presence of a susceptibility to a
mood disorder or related disorder of said individual.

         34. A method as in claim 33 wherein said protein
35 is detected with an antibody which is capable of

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recognising a string of at least 8 continuous glutamines.

35. A method as in claim 34 wherein said antibody is mAB 1C2.

36. A nucleic acid as claimed in claim 21 for use as a medicament in the treatment of a mood disorder or related disorder.

37. A protein as claimed in claim 23 for use as a medicament in the treatment of a mood disorder or related disorder.

38. A pharmaceutical composition which comprises a nucleic acid as claimed in claim 21 and a pharmaceutically acceptable carrier.

39. A pharmaceutical composition which comprises a protein as claimed in claim 23 and a pharmaceutically acceptable carrier.

40. An expression vector which comprises a sequence of nucleotides as claimed in claims 21 or 22.

41. A reporter plasmid which comprises the promoter region of a nucleic acid molecule as claimed in claim 21 or 22 positioned upstream of a reporter gene which encodes a reporter molecule so that expression of said reporter gene is controlled by said promoter region.

42. A cell line transfected with the expression vector of claim 40.

43. An eukaryotic cell or multicellular tissue or organism comprising a transgene encoding a protein as claimed in claims 23 or 24.

5   44. A method for determining if a compound is an enhancer or inhibitor of expression of a gene associated with a mood disorder or related disorder which comprises the steps of:

10   a) contacting a cell as claimed in claim 42 with said compound;

            b) detecting and/or quantitatively evaluating the presence of any mRNA transcript corresponding to a nucleic acid as claimed in claim 21
15   or 22; and

            c) comparing the level of transcription of said nucleic acid with the level of transcription of the same nucleic acid in a cell as claimed in claim
20   42 not exposed to said compound;

       45. A method for determining if a compound is an enhancer or inhibitor of expression of a gene
25   associated with a mood disorder or related disorder which comprises the steps of:

            a) contacting a cell as claimed in claim 42 with said compound;

30   b) detecting and/or quantitatively evaluating the expression of a protein as claimed in claims 23 or 24 and

35   c) comparing the level of expression of said

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protein with that of the same protein in a cell not exposed to said compound.

46. A method for determining if a compound is an enhancer or inhibitor of expression of a gene associated with a mood disorder or related disorder which comprises the steps of:

a) contacting a cell transfected with a reporter plasmid as claimed in claim 41 with said compound;

b) detecting or quantitatively evaluating the amount of reporter molecule expressed; and

c) comparing said amount with the amount of expression of said reporter molecule in a cell comprising said reporter plasmid and not exposed to said compound.

47. A compound identified as an enhancer or an inhibitor of the expression of a gene associated with a mood disorder or related disorder by a method as claimed in claims 44 to 46.